

REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claims 2 – 10, 13, 14, 16, 18, 19, 22 – 24, 29, 30, 32, 35, 36, 40 and 41 are cancelled.

Claims 1, 11, 12, 15, 17, 20, 25, 26, 27, 33, 34 have been amended.

No claims have been added.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims as set forth above, claims 1, 11, 12, 15, 17, 20, 21, 25 – 28, 31, 33, 34 and 37 – 39 are now pending in this application.

A. Rejection of claims 1, 2, 11, 12, 15 – 17 and 20 – 25 under 35 U.S.C. § 112, first paragraph

On page 2, of the Office Action the Examiner has rejected claims 1, 2, 11, 12, 15 – 17 and 20 – 25 under 35 U.S.C. § 112, first paragraph. Applicants address the Examiner's rejections and rejection withdrawals in the order 1) through 5), as they appear on pages 2 – 4 of the Office Action.

1) The Examiner alleges that claims 1, 11, 12 and 15 contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. The Examiner has taken the position that there is “no compound [that] has yet [been] shown [to have] clinical efficacy against every type of cancer.” The Examiner also asserts that “there is no basis for the treatment of a serine/threonine protein kinase related disease in the specification, nor is there any testing to indicate that compounds of the instant invention are effective in the treatment of a serine/threonine kinase related disease.”

As an initial matter, Applicants point out that they are not claiming “clinical efficacy against *every* type of cancer—especially in the claims as amended. Instead, Applicants are claiming the treatment of specific diseases set forth in original claim 23—this, not in acquiescence of the Examiner’s position, but simply in an effort to expedite prosecution of this application.

Applicants next address the Examiner’s unfounded assertion that “there [is not] any testing to indicate that compounds of the instant invention are effective in the treatment of a serine/threonine kinase related disease.”

First, Applicants point out that it is well settled that *in vitro* data is sufficient, in many cases, to satisfy the utility and the enablement requirement of 35 U.S.C. § 112, first paragraph. *See Cross v. Iizuka*, 224 U.S.P.Q. 739 (Fed. Cir. 1985). Applicants assert that the *in vitro* data disclosed in the specification at pages 77, 81, 86, 90 and 91, is, in fact, sufficient to satisfy the utility and the enablement requirements of 35 U.S.C. § 112, first paragraph.

Second, the *in vitro* data disclosed in the aforementioned pages of the specification clearly demonstrate that many of the inventive compounds inhibit RAF: a protein kinase that has been unquestionably implicated in the development and maintenance of certain human malignancies. *See* specification at page 3, lines 10 – 16 where Monia *et al. Nat. Med.* 2: 668 – 75 (1996) (already of record) is cited. *See also*, specification at page 51 lines 2 – 4 where it is mentioned that “mutations in RAF’s amino acid sequence have been associated with tumors and cancers.” As the Examiner will note, the data suggest that some of the inventive compounds are indeed very potent inhibitors of RAF. *See*, for example compound A-13, which has an IC₅₀ of 0.1 μM.

Applicants assert that the skilled artisan would conclude from the discussion in the specification and the *in vitro* data mentioned above, that the inventive compounds are indeed useful in the treatment of certain human tumors and cancers because they, in fact, inhibit RAF. Moreover, from the disclosure on page 52, lines 5 – 11, the skilled artisan would infer that the inventive compounds probably exhibit an even more general activity spectrum: “[b]ecause RAF exhibits significant amino acid homology to other serine/threonine protein kinases, the

quinazoline-based compounds of the invention may likely inhibit serine/threonine protein kinases other than RAF.” In other words, the inventive compounds may inhibit many more serine/threonine protein kinases other than RAF, and thus may be useful in treating many tumors and cancers in addition to those claimed.

Since Applicants have shown that claims 1, 11, 12 and 15 contain subject matter which was, in fact, described in the specification in such a way as to enable one skilled in the art to make and/or use the invention, reconsideration and withdrawal of this rejection are respectfully requested.

2) Applicants acknowledge that the Examiner has withdrawn the rejection of claims 17 and 20 – 25 set forth in paragraph 5 of the January 29, 2003 Office Action.

3) Applicants rely on the arguments presented in section 1) above to overcome the rejection set forth in item 3), on page 3 of the Office Action vis-à-vis claims 17, 20, 21, 23 and 25 allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. Notwithstanding the fact that Applicants do not agree with the positions that the Examiner has taken and simply in an effort to expedite the prosecution of this application, Applicants amended claim 17 such that it recites specific diseases and conditions originally set forth in original claim 23.

Reconsideration and withdrawal of this rejection are respectfully requested.

4) Applicants acknowledge that the Examiner has withdrawn the rejection of claim 27 set forth in paragraph 7 of the January 29, 2003 Office Action.

5) Applicants acknowledge that the Examiner has withdrawn the rejection of claims 1, 2, 11, 17, 21 – 27, 33, 34 and 37 – 39 set forth in paragraph 8 of the January 29, 2003 Office Action.

B. Rejection of claims 1, 2, 11, 17, 21 – 27, 33, 34 and 37 – 39 under 35 U.S.C. § 112, Second Paragraph

On pages 4 and 5 of the Office Action the Examiner has rejected claims 1, 2, 11, 17, 21 – 27, 33, 34 and 37 – 39 under 35 U.S.C. § 112, second paragraph.

Firstly, Applicants acknowledge that the Examiner has withdrawn the rejection of the above-mentioned claims set forth in paragraphs labeled 9a) – 9m) and 9o) – 9t) of the January 29, 2003 Office Action.

Second, the Examiner has maintained the rejection set forth in the paragraph labeled 9n) of the January 29, 2003 Office Action. In light of the amendments to claims 15 and 20, this rejection is moot. Specifically, claims 15 and 20 have been amended such that they are independent. Reconsideration and withdrawal of this rejection are respectfully requested.

C. Rejection of claims 26 – 28 and 31 – 33 under 35 U.S.C. § 102

On page 5 of the Office Action, the Examiner rejected claims 26 – 28 and 31 – 33 under 35 U.S.C. § 102 as allegedly being anticipated by Shenoy, et al. (U.S. Patent No. 6,248,771).

In light of the amendments to claim 31, this rejection has been overcome. Applicants have excluded compound A-19, found on page 32 of the specification, from the scope of claim 31. *See In re Johnson* 558 F.2d 1008 (1977) (finding written description support for claim amendment to exclude species recited in application). Reconsideration and withdrawal are respectfully requested.

D. Rejection of claims 26 – 28 and 31 – 33 under 35 U.S.C. § 103

Applicants acknowledge the withdrawal of the rejection of claims 26 – 28 and 31 – 33 under 35 U.S.C. § 103 set forth in the January 29, 2003 Office Action.

E. Rejection of claims 1, 23, 26, 27, 33, 34 and 37 - 39 under 35 U.S.C. § 112, first paragraph

On pages 6 and 7 of the Office Action the Examiner has rejected claims 1, 23, 26, 27, 33, 34 and 37 - 39 under 35 U.S.C. § 112, first paragraph. Applicants address the Examiner's rejections in the order a) through f), as they appear on pages 6 and 7 of the Office Action.

a) Benzyl allegedly not described within genus of formulae I and III

While not acquiescing to the Examiner's position, and simply in an effort to expedite the prosecution of this application, Applicants amended claim 1 such that it does not recite "benzyl" as a possible variable under $R_1 - R_9$. Reconsideration and withdrawal of this rejection are respectfully requested.

b) $-OX_7$, where X_7 is hydrogen, saturated or unsaturated alkyl or a five-membered or six-membered aryl or heteroaryl ring moiety allegedly not described within genus of formulae I and III

Applicants respectfully traverse this rejection on the grounds that $-OX_7$, where X_7 is hydrogen, saturated or unsaturated alkyl or a five-membered or six-membered aryl or heteroaryl ring moiety, is described on page 23, lines 10 – 13 of the specification, in the context of the genera of formulae I and III. Reconsideration and withdrawal of this rejection are respectfully requested.

c) Z' where the ring is optionally substituted with one, two or three alkyl, halogen, trihalomethyl, carboxylate, and ester moieties allegedly not described within genus of formula III

Applicants respectfully traverse this rejection on the grounds that Z' , where the ring is optionally substituted with one, two or three alkyl, halogen, trihalomethyl, carboxylate, and ester moieties, is, in fact, described on page 23, line 23 to page 24, line 1 of the specification in the context of the genus of formula III. Reconsideration and withdrawal of this rejection are respectfully requested.

d) – f) Exclusion of provisos

On page 7 of the Office Action, the Examiner points out that certain provisos were excluded, which affect claims 26, 27, 33, 34 and 37 – 39. Applicants note that the provisos were inadvertently excluded in the previous response. Applicants have added the provisos where appropriate. Reconsideration and withdrawal of this rejection are respectfully requested.

F. Rejection of Claims 1, 11, 17, 20, 21, 23, 25 – 27, 33, 34 and 37 – 39 under 35 U.S.C. § 112, Second Paragraph

On pages 8 and 9 of the Office Action the Examiner has rejected claims 1, 11, 17, 20, 21, 23, 25 – 27, 33, 34 and 37 – 39 under 35 U.S.C. § 112, second paragraph. Applicants address the Examiner's rejections in the order a) through i), as they appear on pages 8 and 9 of the Office Action.

a) Not known what is meant by definition of X_7 , where X_7 is a five-membered aromatic ring

While not acquiescing to the Examiner's position, and simply in an effort to expedite the prosecution of this application, Applicants amended the definition of X_7 in OX₇ in claims 1, 11, 15, 20, 27 and 31 such that the aromatic ring in the definition of X_7 may only be a six-membered aromatic ring. Reconsideration and withdrawal of this rejection are respectfully requested.

b) Alleged double inclusion of trihalomethyl by using $C(X_6)_3$

While not acquiescing to the Examiner's position, and simply in an effort to expedite the prosecution of this application, Applicants deleted $C(X_6)_3$ in claims 11 and 27. Reconsideration and withdrawal of this rejection are respectfully requested.

c) – d) Not known what is meant by “A₄and” and “andA₅”

As the Examiner rightly points out, spaces are needed in “A₄and” and “andA₅” in claims 17 and 26. Accordingly, Applicants have amended claims 17 and 26 so that there is a space between “A₄” and the word “and.” Likewise, Applicants have amended claims 17, 26 and 34 so that there is a space between the word “and” and “A₅.” Reconsideration and withdrawal of this rejection are respectfully requested.

e) Insufficient antecedent basis in claim 20 for X₇ in OX₇ is hydrogen, saturated or unsaturated alkyl or a five-membered or six-membered aryl or heteroaryl ring moiety in the definition of R₆, R₇, R₈ and R₉ (currently amended as R₃, R₄, R₅ and R₆)

This rejection has been overcome by making claim 20 an independent claim. Moreover, there is sufficient antecedent basis in the specification in the context of compounds of formula X for -OX₇, where X₇ is hydrogen, saturated or unsaturated alkyl or a five-membered or six-membered aryl or heteroaryl ring moiety, on page 29, lines 13 – 16 of the specification. Reconsideration and withdrawal of this rejection are respectfully requested.

f) Not know what is meant by X₁₃ and X₁₄ is a five membered aryl

While not acquiescing to the Examiner's position, and simply in an effort to expedite the prosecution of this application, Applicants amended the definition of X₁₃ and X₁₄ in claims 26 and 34 such that the aromatic ring in the definition of X₁₃ and X₁₄ may only be a six-membered aromatic ring. Reconsideration and withdrawal of this rejection are respectfully requested.

g) "Pyrrole" with respect to formula I

This rejection has been overcome by the amendments to claims 26 and 27. These claims now exclude the pyrrole compound at the end of the claim by referring only to compounds of the formula III. Reconsideration and withdrawal of this rejection are respectfully requested.

h) Not known what is meant by "arylring"

As the Examiner rightly points out, a space is needed in "arylring" such that it reads "aryl ring" instead. Applicants have amended claim 27 accordingly. Reconsideration and withdrawal of this rejection are respectfully requested.

i) Claims 25 and 33 depend from a cancelled claim

Applicants have amended claim such that neither claim depends from a cancelled claim. Reconsideration and withdrawal of this rejection are respectfully requested.

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended are respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

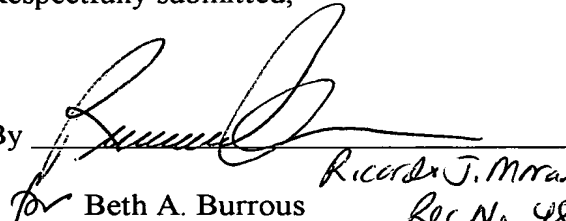
The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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